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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,098	06/20/2003	Sean D. Monahan	Mirus. 013.03.2	7733

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EXAMINER	
SHEN, WU CHENG WINSTON	
ART UNIT	PAPER NUMBER
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/600,098	MONAHAN ET AL.	
	Examiner	Art Unit	
	Wu-Cheng Winston Shen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,15-21 and 23-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,15-21, and 23-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner prosecuting this case has changed. All inquiries directed to the application should be directed to examiner W. - C. Winston Shen.

This application 10/600,098 was filed on June 20. As indicated in the first line of amended specification filed on 07/19/2004, this application is a divisional of non-provisional application US Serial No. 09/447,966, filed November 23, 1999, which is a Continuation-In-Part from non-provisional application 09/391,260, filed September 7, 1999 which is a Divisional from non-provisional application 08/975,573, issued as U.S. Patent 6,265,387, which is a Continuation from 08/571,536, filed December 13, 1995, abandoned.

Claims 1-12, 14, and 22 are canceled.

Status of claims: Claims 13, 15-21 and 23-29 are currently under examination.

Claim Rejection - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. The previous rejection of claims 13-29 under 35 U.S.C. 112, first paragraph has been *withdrawn*. Applicant's arguments filed Oct. 11, 2006 have been fully considered and they are persuasive.

Specifically, applicants have amended claims 13 and 16 to recite a process for analyzing gene function comprising: a) injecting a naked polynucleotide encoding the gene into a blood vessel lumen, in vivo; b) increasing *permeability in the blood vessel*, c) delivering the naked polynucleotide to an extravascular cell outside of the blood vessel *via the increased permeability, wherein the gene is expressed*; and d) *analyzing the effects of expression of the gene on the cell.*

The following new grounds of rejection under first paragraph of 35 U.S.C 112 have been necessitated by applicants' amendments to the claims:

Claim Rejection - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 13, 15-21, and 23-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No

amendment shall introduce **new matter** into the disclosure of an application after the filing date of the application".

Claims 13, 15-21, and 23-29 are directed to a process for *analyzing gene function* comprising recited steps.

The specification, originally filed on 06/20/2003 and subsequent amendments to the specification filed on 08/01/2003, 07/19/2004, provided no implicit or explicit support for "*analyzing the effects of expression of the gene on the cell*" as stated in the amended claim 13, and "*analyzing the effects of decreased expression of the gene on the cell*" as stated in amended claim 16, filed on October 11, 2006. Claim 15 depends from claim 13 and claims 17-21, and 23-29 depend from claim 16. Accordingly, the amended claims 13, 15-21, and 23-29 encompass analyzing any effects of expression of any gene.

The specification has only provided support for "Enhancement of *in vivo* gene expression by M-methyl-L-arginine (L-NMMA) following intravascular delivery of naked DNA", and "Enhancement of *in vivo* gene expression by aurintricarboxylic Acid (ATA) delivery enhancer following intravascular delivery of naked DNA. More specifically, the reporter luciferase expression was analyzed (See bridging paragraph from page 12 to page 13 and lines 14-22, page 13). Therefore, the specification fails to provide written description support for the amended claims 13, 15-21, and 23-29, filed on October 11, 2006.

Applicants are reminded that it is their burden to show where the specification supports any amendments to the claims. See 37 CFR 1.121 (b)(2)(iii), the MPEP 714.02, 3rd paragraph, last sentence and also the MPEP 2163.07, last sentence.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure.*

3. Claims 13, 15-21, and 23-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 13, 15-21, and 23-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the applicants have amended claims 13 step d) to recite, "analyzing the effects of expression of the gene on the cell", and applicants have also

amended claim 16 step d) to recite, "analyzing the effects of decreased expression of the gene on the cell".

It is noted that the specification fails to disclose correlation(s), if any, between "analyzing gene function" and "analyzing the effects of expression of the gene on the cell" as recited in claim 13. Similarly, the specification also fails to disclose correlation(s), if any, between "analyzing gene function" and "analyzing the effects of decreased expression of the gene on the cell" as recited in claim 16.

More specifically, it is stated that "Then, delivering the polynucleotide to the parenchymal cell thereby altering endogenous properties of the cell." on page 3 lines 9-10 of the specification, and it is further stated that "A polynucleotide can be delivered to a cell to express an exogenous nucleotide sequence, to inhibit, eliminate, augment, or alter expression of an endogenous nucleotide sequence, or to express a specific physiological characteristic not naturally associated with the cell. Polynucleotides may be coded to express a whole or partial protein, or may be anti-sense." on page 9 lines 10-13 of the specification. These assumed supports, indicated by applicants in the reply filed on Oct. 11, 2006, for amended claims 13 and 16, does not teach *analyzing gene function* as recited in the preamble of claims 13 and 16.

Accordingly, the specification only teaches delivery of polynucleotide in the cell results in alteration of gene expression. Therefore, the specification fails to provide any specific guidance or working examples to enable a skilled person in the art, to which it pertains, or with which it is most nearly connected, to correlate the information regarding analyzing the effects of expression of the gene on the cell with analyzing gene function, and thereby to make and/or use the instant invention.

It is worth noting that analysis of gene expression is not equivalent to analysis of gene function. Relevant to this subject matter, the specification disclosed enhanced expression of a reporter gene encoding luciferase following intravascular delivery of naked DNA (See examples, paragraphs [0055] and [0056]). However, the specification fails to disclose any gene function of luciferase or any analysis of the effects of luciferase expression on any endogenous gene function *in vivo*.

Therefore, there appears to be a lack of teachings in the specification correlating the information regarding analyzing the effects of expression of the gene on the cell with the analyzing gene function, and thereby an artisan cannot make and use the invention of a process for analyzing gene function as claimed in the instant application.

The following new grounds of rejection under second paragraph of 35 U.S.C 112 have been necessitated by applicants' amendments to the claims:

Claim Rejection - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 26 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. *This rejection is necessitated by the cancellation of claim 22.*

Claims 26 and 27 depend from a cancelled claim, claim 22. Therefore, it is unclear what is/are encompassed by claims 26 and 27

5. Claims 13, 15-21, and 23-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13 and 16 is indefinite because *it lacks a positive active step relating back to the preamble.* The preamble recites "a method for *analyzing gene function*", however the last positive active step is drawn to "*analyzing the effects of expression of the gene* on the cell". Therefore it is unclear as to whether the method is drawn to "a method for *analyzing gene function*" or "a method of analyzing the effects of *expression of the gene* on the cell".

It is emphasized that *analyzing the effects of expression of the gene* on *the cell*, as recited in step (d) of claims 13 and 16, is not the same as *analyzing gene function,* as recited in the preamble of claims 13 and 16. As stated in the rejection under 32 U.S.C. 112, first paragraph, in the proceeding section, analysis of gene expression is not equivalent to analysis of gene function. Relevant to this subject matter, the specification disclosed enhanced expression of a reporter gene encoding luciferase following intravascular delivery of naked DNA (See examples, paragraphs [0055] and [0056]). However, the specification fails to disclose any gene function of luciferase or any analysis of the effects of luciferase expression on any endogenous gene function *in vivo*.

Double Patenting

6. The terminal disclaimer filed on Oct. 11, 2006 regarding double patenting between instant application and U.S. Patent No 6,627,616 issued on Sep. 30, 2003 has been received and thereby the nonstatutory double patenting rejection is *withdrawn*.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

8. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30

PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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